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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,423	03/20/2001	Richard Henry Jones	Q62257	7786
7590	12/18/2003		EXAMINER	
Sughrue Mion Zinn Macpeak & Seas 2100 Pennsylvania Avenue NW Washington, DC 20037-3202			AUDET, MAURY A	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/719,423	JONES ET AL.
	Examiner Maury Audet	Art Unit 1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 September 2003.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-7 and 10-15 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-7 and 10-15 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

This action is responsive to the amendments filed on 7/9/03 and 9/2/03. Claims 1-7 and 10-15 are under examination on the merits. The action is made non-final based on the new rejections of the method claims (12-15), under 35 U.S.C. § 112 1<sup>st</sup> ¶, and additional nonstatutory “Double Patenting” rejection using a new reference; both inadvertently omitted from the previous office action (see below).

### ***Specification/Claim Objections***

The objections to the specification page 6, lines 19, 21, 32, and 35; and page 7, lines 2 and 5 (125-Insulin misnomer); claim 11 (misspelling); and abstract (missing) are all withdrawn subsequent to applicant’s amendment thereof.

### ***Claim Rejections - 35 USC § 112 1st***

The rejection of claims 1-7, and 10-15, under 35 U.S.C. 112, 1<sup>st</sup> ¶ (scope) is withdrawn due to applicant’s amendment thereof.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 1-7, and 10-15, under 35 U.S.C. 103, is withdrawn pursuant to applicant’s arguments, which were persuasive.

## ***NEW REJECTIONS***

### ***Claim Rejections - 35 USC § 112 1<sup>st</sup> ¶, Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988)). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for a method of using the insulin-rT3 compounds of the present invention for insulin replacement therapy (i.e. diabetes) or the following reasons.

*The nature of the invention:* The claimed invention is drawn to a method of using the insulin-rT3 compounds of the present invention for insulin replacement therapy (i.e. diabetes).

*The state of the prior art and the predictability or lack thereof in the art:*

The art teaches that the efficacy of therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective plasma concentrations, solubility in tissues, biotransformation, toxicity, proteolytic degradation, immunological inactivation, rate of excretion or clearance (half-life), deactivation by the liver, hydrolysis in serum, binding to plasma protein, and in the case of antivirals, propensity for emergence of resistant strains (see Benet et al., pp. 3-32, in The Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21 and footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO BD> APP>& Inter. 1992)).

*The amount of direction or guidance present and the presence or absence of working examples:* Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification does not teach the in vivo use of the insulin-rT3 compounds for insulin replacement therapy (i.e. diabetes). Therefore, it is unclear whether the compounds are capable of insulin replacement therapy, for instance in diabetes.

*The breadth of the claims and the quantity of experimentation needed:* Given the extensive list of biological factors that must be met in order for a therapeutic to be shown effective (as discussed in Benet et al.) and absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art; namely as to whether the compounds can actually effectively replace insulin in such diseases as diabetes; it would require undue

experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 and 10-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, and 5-12 of Jones et al. (5,854,208; hereafter **Jones et al. '208**) in view of Ikeda et al. Applicant's arguments (7/9/03, page 6) have been fully considered but they are not found persuasive. The rejection is **also** maintained here in view of Weeks et al. (to further clarify that rT3 is a thyroid hormone as well as a thyroxine derivative; as discussed in the previous action under 35 U.S.C. § 103).

Claims 1-7 and 10-15 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of Jones et al.

(6,063,761; hereafter **Jones et al.** '761; a divisional of Jones et al. '208) in view of Ikeda et al. or Weeks et al.

Jones et al. '761 teach the same compounds of Jones et al. '208 in a method of use for treating diabetes.

Applicants have argued that there is a surprising advantage [i.e. unexpected results] in the performance of the rT3 conjugate over the T4 conjugate. However, the advantage is based on the fact that rT3 is inactive and will not also stimulate the thyroid, which is a known property of rT3. Furthermore, no unexpected results have been shown in vivo (as discussed above). And even if such were shown in this case, and as Weeks et al. teach above, rT3 is known to be the inactive form of rT3 (**"this form of T3 ["reverse T3"] formed by target cells is biologically inactive, monodeiodination to form "reverse T3" provides a mechanism to attenuate the metabolic effects of thyroid hormones"** (page 2)(emphasis added)), and thus would be *expected* to not stimulate the thyroid (Applicant's asserted unexpected result). The invention uses any thyroid hormone, rT3 or otherwise, to allow greater hepatoselectivity of the insulin molecule. If not obvious based on the Jones et al. '208 claims themselves (i.e. claims 3-4), it would have been obvious to one of ordinary skill in the art at the time the invention was made to use rT3 covalently bound to the Jones et al. '208 insulin, in view of any of Weeks et al., or the previously discussed Ikeda et al., because rT3 is known to not stimulate the thyroid hormone, yet retains hepatoselectivity like any other thyroid hormone/thyroxine derivative. Thus, using rT3 with insulin would have the known advantageous end result of improving the insulin hepatoselectivity and bioavailability without thyroid stimulation.

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From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***Conclusion***

Due to the new grounds of rejection herein, this action is made nonfinal.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA

December 10, 2003

*Brenda Brumback*  
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